SUBJECT INDEX

Acetaldehyde effects
  adverse effects 17
  lipid peroxidation 21, 22
  microtubules 18
  mitochondria 19, 20
  vicious cycle 20
Acivicin
  clinical trials 246
  mechanism of action 244, 245
  resistance 245
  structure 244
Adverse drug reactions
  β-blockers 163–88
  β-receptor partial agonists 223–30
  phenytoin 345
Ageing, opioid system 400, 401
L-Alanosine
  antitumor activity 255
  clinical studies 257, 258
  mechanism of action 254
  metabolism 255–57
    scheme 256
  structure 254
Alcohol *see* Ethanol
Alcohol dehydrogenase 5
  -mediated toxicity 7–9
Alcoholics and xenobiotic toxicity 5–7
Alzheimer's disease, opioid system 398–400
Amino acid analog, anticancer agents 243–62
Angina, β-receptor partial agonists 216, 217
Animal experiments, lung nitrosamine effects 96–100
Animal models
  anxiety 321–35, 361–63
  anxiety-depression 363, 364
  depression 364
  neurological disorders 396
Anticancer agents, amino acid analog 243–62
Antidepressant drug action
  animal studies 43–46
  contrast effects 316
  extinction effects 313, 314
  human studies 46–49
  5-hydroxytryptamine effects 43–49
Antimalarial drugs, enantiomers 285, 286
Anxiety
  animal models 321–35
  defensive behavior 332
  drugs altering 324
  observer-rated 331
  trait and state 322
Anxiety and panic disorders
  exploratory behavior tests 324–29
  generalized 323, 324
  social behavior tests 329–31
Anxiolytic effects
  contrast effects 314–16
  extinction 310–13
Apamin
  potassium channel toxin 147–50
  structural features 148
Arachidonic acid metabolism 59
Arrhythmias, β-receptor partial agonists 218–20
Arthritic disorders, enantiomers 273–88
2-Arylpropionic acids
  arthritic disorders 275–80
  enantiomers 276
  inversion clearance 279
  inversion sites 277
  metabolic pathways 278
  R and S plasma concentrations 276, 277
  structures 275
L-Aspartic acid analogs, anticancer effects 251–58
Asthma, β-blocker effects 227
Autoinhibition 431
Azaserine
  antitumor activity 250
  clinical trials 250, 251
  mechanism of action 249
  metabolism 250
  structure 249

Bacteria, gut distribution 70–72
Behavioral changes and stressors 124–30
  shuttle task 125–27
β-Adrenoceptor antagonists metabolism 385
β-Blockers
  blood–brain barrier 165–71
  CNS effects in man 168–71
  CNS effects in patients 172–80
  CNS side-effects 163–88
  CSF concentration 166
  distribution coefficients 164
    model 164
  memory effects 182–88
  pharmacokinetics 164, 165
  side-effects 168–70
  structure–activity relationship 206
Blood pressure, β-receptor partial agonist 213–15
α-Bungarotoxin, potassium channel 139–41
L-Buthionine-S,R-sulfoxime
  antitumor activity 260, 261
  mechanisms of action 260, 261
  metabolism 261, 262

Calcitonin gene-related peptide
  blood vessel effects 446
  distribution 443
  perivascular nerve 443–46
  uterine artery 445
Cancer, origin 469
Carcinogenesis
  cell transformation 474–77
  mechanisms *in vitro* 473–78
  mechanisms *in vivo* 472, 473
  multistep 469–80
    clinical evidence 478, 479
    genetics 470–72
    stages 480

Carcinogens, metabolic activity in gut 85, 86
Carcinoma, colorectal; multistep progression 479
Cardiac output, β-receptor partial agonists 212, 213
Charybdotoxin
  amino acid sequence 151
  potassium channel toxins 152–54
Cirrhosis production 24–27
Collagen disorders
  accumulation 25, 26
  and ethanol 24–27
Congeners, role in ethanol effects 23
Contrast effects
  antidepressant effects 316
  anxiolytic effects 314–16
  definition 309, 314
Cytochrome P-450
  ethanol metabolism 2–4
  immunohistochemistry and alcoholism 9
Cytochrome P-450IID1
  autoantibodies 301–303
  cloning of human 303
  deficiency 300, 301
  immunoquantitation 301
  mutant detection 303–306
Cytotoxic drug enantiomers 287, 288

Debrisoquine 380
Debrisoquine/sparteine metabolism
  drug deficient metabolism 299
  genetic polymorphism 297, 306, 377–90
    molecular mechanisms 298–306
    racial differences 388
  phenytoin metabolism 344
Dendrotoxins
  amino acid sequence 147
  potassium channel 141–43
    blockade 142
Depression, opioid system 412–14
DFMO
  anticancer activity 258
  clinical trials 259, 260
  structure 258–60
L-DON
  antitumor activity 247
  clinical studies 248, 249
  mechanism of action 246, 247
  metabolism 248
  resistance 247, 248
  structure 246
Dopamine, stressor effects 122
Drug
  asymmetric 274
  deficient metabolism and debrisoquine 299
  gut wall metabolism 67–86
  metabolizing enzyme deficiency 300
Drug development, polymorphic oxidation 388–90
Drug glucosidation 53–55
Drug interactions and metabolism 387
Drug metabolism
  enzyme study methods 352
  ethnic variations 387, 388

Enantiomers
  arthritic disorders 273–88
  terminology 274, 275
Encamide metabolism, genetic polymorphism 382
Endothelial cells, peptide effects 448–50
Enolic acids, structures 280, 281
Epilepsy, opioid system 404–406
Ethanol (alcohol)
  hepatic injury mechanism 1–28
  hepatocyte oxidation 3
Extinction
  antidepressant effects 313, 314
  anxiolytic effects 310–13
  definition 309

Fatty liver
  appearance 15
  fibrosis 15, 16
  mechanisms 9–12
  perivenular fibrosis 14, 15
  perivenular injury 12–14
Flecamide metabolism, genetic polymorphism 380–82

Genes
  carcinogenesis 471
  tumor suppressor 477, 478
Genetic polymorphism 350, 351
  debrisoquine/sparteine metabolism 297–306, 377–90
  definition 351
  drug response studies 352–54
  poor drug metabolism 378, 379
Glucosidation pathway
  biological characteristics 55
  drugs 53–55
L-Glutamine analogs, anticancer effects 244–51
Glycosides, urinary drug structures 54
Gold, drug enantiomers 286, 287
Gut
  antimicrobial drug effects 73, 74
  bacterial distribution 70, 71
  ethanol injury 2
  lumen drug metabolism 68, 69
    drugs metabolized 80–84
    study methods 74, 75
  microflora metabolism 71–73
  pH 69
Gut wall
  drug metabolism 67–86
    enzymes 74
    hydrolysis 77
    phase II reactions 76
    study methods 75–80
  drugs metabolized 80–84

Heart failure, β-receptor partial agonists 220–22
Heart rate, β-receptor partial agonists 209–12
Hepatic injury, ethanol mechanism 1–28
Holeboard test, anxiety 326, 327
Huntington's disease, opioid system 401, 402
Hybrid lipid 278
5-Hydroxyindoleacetic acid (5-HIAA), antidepressants and CSF 48
5-Hydroxytryptamine (5-HT)
  antidepressant effects 46, 47
  function and antidepressants 47
Hypertension, β-receptor partial agonists 216
Hypothalamic–pituitary–adrenal hormones 357–68
  antidepressant effects 365–67

anxiety changes 359, 360
hormones 357–68
anxiolytic effects 365–67
depression changes 360, 361
exogenous in anxiety and depression 364, 365

Immunological effects, ethanol 23
Immunomodulating drugs, enantiomers in arthritis disorders 281–85
Inflammation and leukotrienes 57–63
Intermittent claudication, β-receptor partial agonists 222

Leiurotoxin, potassium channel 154
Leukotrienes
biosynthesis 58, 59
and inflammation 57–63
metabolism 59
Levamisole enantiomers 285
Light-dark transition 328, 329
anxiolytic profile 332
Lipoxygenase products, inflammation generation 61
Lung, nitrosamines 95–101

Mania, opioid system 412–14
MCD peptide and potassium channel 143–146
A cell response 144, 145
interaction 146
Memory, β-blocker effects 182–88
3-Methylindole
induced pneumotoxicity 105–16
lung disease 106
metabolism 106, 107
metabolites 107–10
phospholipid biosynthesis 113
prostaglandin H synthase activation 110–12
radical formation 108–10
surfactant effects 114
tissue-specific changes 112–15
Metronidazole, gut metabolism 82
Mutagens, metabolic activation in gut 85, 86
Mutant, cytochrome P-450IIDI detection 303–306

Neuroleptic metabolism 385, 386
Neuroleptic-induced movement disorders, opioid system 403, 404
Neuropeptides
blood vessel localization 446
perivascular plasticity 450–53
vascular tone 451
vasomotor mechanism 429–53
Neuropeptide Y
axon electron microscopy 434
blood vessel effects 436
perivascular nerves 433–36
vascular actions 432
Neurotransmission, 5-HT and antidepressants 45
Nitrosamines
animal experiments 96–100
cell studies 100, 101
lung 95–101
metabolism 96
Nonsteroidal anti-inflammatory drugs, asymmetric in arthritis 275–81
Norepinephrine, stressor effects 120, 121

Noxiustoxin
amino acid sequence 151
potassium channel toxin 150–52
Nutrition and liver disease 27, 28

Obsessive–compulsive disorder 334
Open field test in anxiety 325, 326
Opioid peptides
perivascular nerves 447
structures 397
Opioid system
families 396
psychiatric disorders 395–415
treatment 414

PALA
antitumor activity 252
clinical studies 252–54
mechanism of action 251, 252
metabolism 252
Parkinson's disease, opioid system 402, 403
Partial agonist activity
adverse reactions 225–30
assessment 204–207
bronchoconstriction 226, 227
concept 203
molecular structural requirements 203
pharmacodynamics 209
plasma lipids 229, 230
rebound 228, 229
D-Penicillamine
enantiomers 281, 282
pharmacokinetics 283
toxicity 282
Perhexiline metabolism 384
Peripheral resistance, β-receptor partial agonists 215, 216
Pharmacogenetics
and classical genetics 350
definition 349
genome mapping 351
and molecular genetics 349–55
Phenytoin
impaired hydroxylation inheritance 343, 344
and mephenytoin polymorphism 344
metabolites 342
pharmacokinetics 342, 343
toxicity 345
Phenytoin 4′-hydroxylation 341–45
pathway 342
Phobic disorders, animal models 333, 334
Plus maze test
in anxiety 327, 328
anxiolytic profile 332
Pneumotoxicity, 3-methylindole induced 105–16
mechanism, scheme 115
Polymerase chain reaction 353, 354
Post myocardial infarction, β-receptor partial agonists 217, 218
Post traumatic stress disorder 334
Postural hypotension, β-receptor partial agonists 222, 223
Potassium channel, family 138
Potassium channel toxins 137–55
amino acid sequences 147
interactions 146
Propafenone metabolism 382, 383
N-Propylajmaline metabolism 383, 384
Prostaglandin E_2, analog enantiomers 288
Psoriasis 61

Receptor, β-adreno-
  β_1, receptor affinity/coupling 210
  β_2, receptor affinity/coupling 210
  discovery 201
  features 202
  inhibition 204
  receptor affinity/coupling 208, 209
  responses mediated 201, 202
Receptor, GABA-benzodiazepine and stress 367, 368
Receptors, 5-HT and antidepressants 44, 45
Receptor, opioid
  seizure modulation 407, 408
  subtypes 298
Restriction fragment length polymorphism (RFLP) 354
Rheumatoid arthritis 62

Schizophrenia, opioid system 409–12
Separation vocalization anxiety 331
Social interaction test
  anxiety 330, 331
  anxiolytic profile 333
Southern blotting 353
Sparteine metabolism 380
Spinal cord injury, opioid system 409
Staircase Test, anxiolytic profile 333
Stress, neurotransmitter effects 367
Stressors
  behavioral changes 124–30
  brain stimulation 129, 130
  dopamine 122
  escape latencies 125–27
  genetic response differences 130–32
  individual response differences 130–32
  neurotransmitter changes 119–24
  norepinephrine 120–22
Stroke, opioid system 408, 409
Substance P
  actions 442, 443
  amino acid sequence 440
  fluorescence microscopy 442
  perivascular nerve 440–43
Sulfasalazine, metabolic pathways 84
Sulindac structure 280
Synergism 431

Thalidomide enantiomers 283, 284
Tourette syndrome, opioid system 404

Ulcerative colitis 62

Vascular neuroeffector mechanisms 430–3
Vascular tone, neuropeptide regulation 451
Vasoactive intestinal polypeptide
  blood vessel effects 439
  distribution 436
  perivascular nerve 436–39
Vasomotor mechanisms and peptides 429–53
Virus disease and ethanol 23, 24